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09/990,762	11/14/2001	J. Keith Joung	MTV-030.02	2226

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EXAMINER

SHIBUYA, MARK LANCE

ART UNIT PAPER NUMBER

1639

DATE MAILED: 05/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/990,762

Applicant(s)

JOUNG ET AL.

Examiner

Mark Shibuya

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 10-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>11/04/2003</u> . | 6) <input type="checkbox"/> Other: ____.  |

## **DETAILED ACTION**

### ***Status of the Claims***

1. Claims 1-20 are pending. Claims 10-20 have been withdrawn.
2. Claims 1-9 stand finally rejected.
3. The rejection of claims 1-4 and 6-9 under 35 U.S.C. 102 as being anticipated by U.S. Patent 5,580,736, as set forth in the previous Office action mailed 11/04/2003, is withdrawn in the instant Office action.
4. The rejection of claims 1-9 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,580,736 as applied to claims 1-4 and 6-9, and further in view of Kornacker et al., Molecular Microbiology 30(3):615-624, 1998, as set forth in the previous Office action mailed 11/04/2003, is withdrawn in the instant Office action.
5. Claims 1-9 are rejected newly under 35 U.S.C. § 112, first paragraph and second paragraph.
6. Because applicant's amendments to the claims have necessitated the new rejections, these rejections are made final.

### ***Information Disclosure Statement***

1. The information disclosure statement (IDS) submitted on 9/30/2002 was considered only in part because of missing non-patent references (please see the previous Office action, mailed 11/04/2003). Applicant furnished replacement copies of the missing references on 2/6/2004, placing the submission in compliance with the provisions of 37 CFR 1.97. Accordingly, all references cited by the Applicant's information disclosure statement have been considered by the examiner. IDS citations

to those previously missing references are now initialed on the attached Form 1449 accompanying this Office action.

***Election/Restrictions***

2. This application contains claims 10-20 that are drawn to an invention nonelected with traverse in the Paper filed 9/29/2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Withdrawn Claim Rejections - 35 USC § 102***

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. The rejection of claims 1-4 and 6-9 under 35 U.S.C. 102 as being anticipated by U.S. Patent 5,580,736, and as set forth in the previous Office action mailed 11/04/2003, is withdrawn in the instant Office action.

8. Applicant's arguments, see response to the previous Office action, filed 2/6/2004, p. 7, paragraphs 3-5, with respect to the rejection of claims 1-4 and 6-9 have been fully considered and are persuasive. The rejection of claims 1-4 and 6-9 under 35 U.S.C. 102 has been withdrawn.

9. The rejection of claims 1-4 and 6-9 under 35 U.S.C. 102 has been withdrawn without regard to the amendment of claim 1, filed 2/6/2004. The cited prior art of Brent et al., U.S. Patent 5,580,736, at col. 6, lines 39-43, which states that “[b]ait proteins, via their DNA binding domain, bind to their specific DNA site upstream of a report gene; reporter transcription is not stimulated, however, because the bait protein lacks its own activation domain”, teaches away from the claimed limitation of claim 1, which recites: “a chimeric gene which encodes a fusion protein, including one or more DNA-binding domains, an **activation** domain, and a test polypeptide [emphasis added].”

***Withdrawn Claim Rejections - 35 USC § 103***

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The rejection of claims 1-9 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,580,736 as applied to claims 1-4 and 6-9, and further in view of Kornacker et al., Molecular Microbiology 30(3):615-624, 1998, as set forth in the previous Office action mailed 11/04/2003, is withdrawn in the instant Office action.

11. Applicant's arguments, see Response to the previous Office Action, filed 2/6/2004, p. 8, paragraph 2, with respect to the rejection of claims 1-9 have been fully considered and are persuasive. The rejection of claims 1-9 under 35 U.S.C. 103 has been withdrawn.

6. The rejection of claims 1-9 under 35 U.S.C. 103 has been withdrawn without regard to the amendment of claim 1, filed 2/6/2004. In fact, the cited prior art of Brent et al., U.S. Patent 5,580,736, at col. 6, lines 39-43 teaches away from the claimed

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invention, please see above. Also, the cited prior art of Kornacker et al., *Molecular Microbiology*, (1998) vol. 30 (3), 615-624, which discloses a two-hybrid system, teaches away from the claimed invention by contrasting the system of Kornacker with other *E. coli* two-hybrid systems, noting that "mechanistically, they differ fundamentally from our system," because "the fact that these [other] systems signal protein interactions through activation of a reporter gene rather than repression." Inactivation of the reporter gene teaches away from the claimed limitation of claim 1, which recites: "a chimeric gene which encodes a fusion protein, including one or more DNA-binding domains, an **activation** domain, and a test polypeptide [emphasis added]."

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-9 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for selection of a dimerizing polypeptide using a DNA library at least  $10^7$  members in prokaryotic cells, wherein the cells express a chimeric gene encoding a fusion protein comprising one or more binding domains, an activation domain, and a test polypeptide encoded by the library, and further comprising a reporter gene that is *HIS3*, wherein stringency of the growth advantage conferred by expression of *HIS3* is controlled by 3-aminotriazole (3-AT), and wherein cells expressing library-encoded dimers are isolated by their growth advantage, does not reasonably provide enablement for selection of a dimerizing polypeptide using a DNA library of at least  $10^7$

members in eukaryotic cells, wherein the cells comprise a reporter gene other than *HIS3*, and wherein cells expressing library-encoded dimers are isolated by traits other than growth advantage. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and / or use the invention commensurate in scope with these claims.

9. This rejection is necessitated by applicant's amendment to claim 1, filed 2/6/2004, adding the language ~~i—providing~~ introducing a DNA library into a population of host cells under the conditions . . . .

10. Claims 1-9 are drawn to selecting a dimerizing polypeptide by introducing a DNA library into a population of host cells wherein each host cell contains a chimeric gene encoding a fusion protein, including one or more DNA-binding domains, an activation domain, and a test polypeptide and further contains a reporter gene operably linked to a transcriptional regulatory sequence, including binding sites for the DNA binding domains of the chimeric gene, and wherein binding of a single copy of the fusion protein does not result in a desired level of expression of the reporter gene, whereas dimerization of the fusion protein and binding of that dimerized fusion proteins to the reporter gene results in a desired level of expression whereby the host cell may be isolated thereby and a dimerizing test polypeptide selected. Thus the claims are drawn, to a method for selecting a dimerizing test polypeptide, comprising a library of genes encoding fusion proteins encoding both DNA binding domains and activating domains (unlike traditional two-hybrid systems) and further encoding test polypeptides.

11. The specification contemplates that *E. coli* interaction trap assays have a much higher relative transformation efficiency (typically  $10^9$  or greater) than yeast, so that prokaryotic systems would appear to address the library size restrictions of the yeast systems. The specification states: “[h]owever, although higher transformation efficiencies are possible in *E. coli*, a significant deficiency of the prior art is that it does not make clear which, if any, **reporter genes(s)** have the characteristics required for use in the analysis of libraries larger than  $10^7$  in size.” The specification contemplates that desirable reporter genes should have one or more of the following characteristics:

- 1) The reporter gene should readily facilitate the rapid analysis of very large numbers of candidates.
- 2) The reporter gene system must be sufficiently stringent or selective so that spurious, randomly arising background mutations do not complicate the analysis.
- 3) Expression of the reporter gene should be quantifiable and should easily facilitate the selection of candidates based on any specific criteria.

The specification at pp. 3-4.

The specification at p. 14 contemplates that the reporter gene encode a gene product for a signal that color, fluorescence, luminescence, a cell surface tag, cell viability, relief of a cell nutritional requirement, cell growth and drug resistance. The specification, at p.15, contemplates as an embodiment, the yeast His3 gene as a reporter gene and the control of the stringency of growth advantage by varying concentrations of 3-aminotriazole (3-AT). The specification contemplates, as a second embodiment, a reporter gene that is one of various taught beta-lactamase genes, with control of the growth advantage by beta-lactamase inhibitor and / or beta-lactam



antibiotic. The specification, at p. 15, further suggests ten examples of fluorescent proteins that may be encoded by the reporter gene.

The specification at p. 16, eukaryotic and prokaryotic cells as host cells. The specification at p. 17, contemplates a library of at least  $10^7$ ,  $10^8$ ,  $10^9$ ,  $10^{10}$ ,  $10^{11}$ , or  $10^{12}$ . The specification at p. 21, contemplates screening large libraries of sequences, including  $10^8$ ,  $10^9$ ,  $10^{10}$ , or  $10^{12}$  different sequences. The specification contemplates that the reporter gene encodes a product which confers a growth advantage and is "tunable". The specification, at p. 40, states "[t]o further illustrate this strategy, we have discovered that, **surprisingly**, the HIS3 reporter gene, along with the use of 3AT can be used to rescue a prokaryotic host cell in HIS selective media with sufficient stringency to be able to successfully isolate interacting pairs from a large library of variants."

The specification at pp. 37-38, bridging paragraph, contemplates bait protein constructs for a one hybrid format, wherein "it is not necessary that the transcriptional activation activity be separated from the bait protein into the prey protein, as it is in the two hybrid format. Thus, in a one hybrid format, sequences encoding a known or potential (test) DNA binding domain (DBD), e.g., a polypeptide which may specifically bind to a defined nucleotide sequence of a reporter gene construct[, are] fused in frame to an activation domain, such as a PID."

The specification at p. 58-59, contemplates various known dimerization domains. The specification at pp. 73-74 contemplates identification of dimerizing polypeptides using a chimeric transcription factor containing one or more DNA binding domains fused to a library of random test peptides. Upon dimerization of the transcription factor

leading to two copies of the chimeric transcription factor being bound to the promoter region, transcription of the reporter gene is increased (see Figure 11). The specification at p. 30 defines the term "transcription factor" as any protein that is involved in the initiation of transcription but which is not itself a part of the polymerase. The specification states that factors may interact with other factors, with the RNA polymerase, with the entire complex, with activators, or with DNA. The specification at p. 30, lines 23-24, define the term "activation domain."

The specification 77 to 95, and particularly at p. 81, provides three working example, and especially a two-hybrid system in *E. coli*, using the *HIS3* gene as a reporter, to analyze libraries greater than  $10^8$  in size, for the isolating of genes encoding dimerizing zinc finger proteins.

12. The article of Chien et al., (applicant's reference AK-1, IDS filed 2/06/2004), at p. 9581, para 2, in referring to dimerization and interaction trap assays, states:

**Screening of an Activation Domain Library.** Based on the demonstration of the SIR4-SIR4 interaction in the two hybrid system, we sought to determine whether this or other interactions could be detected by screening a library of total sequences present in the activation domain plasmid. With SIR4 as a fusion with the GAL4 DNA-binding domain, any protein encoded by an activation domain fusion that can interact with SIR might reconstitute GAL4 activity. We note that the library must be constructed in the activation domain plasmid to avoid detecting random (and abundant) sequences that can activate transcription when fused to a DNA-binding domain."

Chien et al., at 9581, para 2.

13. The article of Joung, (applicant's reference AQ-1, IDS filed 2/06/2004), at p. 53, para 2, in part states:

A significant of this *E. coli*-based method relative to the yeast-based system is the ability to assess very large libraries of proteins ( $>10^8$ ) in size for the bacterial system compared with  $10^6 - 10^7$  for the yeast method). This capability results from the extremely high transformation efficiency possible only in bacteria and is particularly useful for the analysis of complex randomized and cDNA libraries. In addition, the method provides an alternative for studying proteins that can not be used in the yeast two-hybrid system (e.g., due to toxicity or poor expression).

Joung at p. 53, para 2.

14. The breadth of the claims encompass a chimeric gene that encodes a fusion protein, including two or more DNA-binding domains, an activation domain and a test polypeptide. The claims encompass selecting for a dimerizing test polypeptide by introducing very large ( $>10^8$ ) DNA libraries into any host cell, including yeast, as well as prokaryotic host cells. The claims encompass a reporter gene operably linked to any transcriptional regulatory sequence, wherein binding of a single copy of the fusion protein to the transcriptional regulatory sequence of the reporter gene does not result in a desired level of expression of the reporter gene. The claims read on dimerization of DNA-binding domains, activation domains or test polypeptides.

15. It would require trial and error screening in order to determine which genes would be capable of acting as reporters. The specification, at pp. 3-4, states that the prior art is deficient as to reporter genes having the characteristics required for the analysis of libraries larger than  $10^7$  in size. The specification at p. 21, states that it was surprising to find that *HIS3* could serve as an appropriate reporter gene in prokaryotic hosts. The

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specification does not disclose examples, working or otherwise, of the use of *HIS3* or any other reporter gene, as usable in a system based on fusion proteins that each have the DNA binding domains, activation domains and test polypeptides. Other detection systems, such as fluorescence activated cell sorting, may be inadequate for the screening of very large libraries, because cell sorting depends upon the individual assessment of single cells.

16. Furthermore, publication of Chien et al. warns against libraries fused to DNA-binding domains because random and abundant sequences can activate transcription. Although the level of skill in the art is high, because of the unpredictability of the art, one of skill in the art would have to pick and choose reporter genes that would work in the claimed invention.

17. Undue experimentation would be required to use DNA libraries larger than  $10^7$  in size in yeast, as encompassed by the claimed invention. The publication of Joung teaches that use of large libraries is possible only because of the extremely high transformation efficiency of bacterial systems. Furthermore, the study of some protein may not be possible in yeast systems, due to toxicity or poor expression. The specification does not provide any working examples of selection of a dimerizing polypeptide using a DNA library of at least  $10^7$  members in eukaryotic cells, wherein the cells comprise a reporter gene other than *HIS3*, and wherein cells expressing library-encoded dimers are isolated by traits other than growth advantage, such as fluorescence activated cell sorting.

18. The instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which experimentation should proceed in carrying out the full scope of the claimed method. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d, 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

19. Claims 1-9 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for lack of Written Description.

20. This rejection is necessitated by applicant's amendment to claim 1, filed 2/6/2004, adding the language i—providing introducing a DNA library into a population of host cells under the conditions . . . .

21. The claims are drawn to selection of a dimerizing polypeptide using a DNA library in host cells, wherein the cells express a chimeric gene encoding a fusion protein

comprising one or more binding domains, an activation domain, and a test polypeptide, and further comprising a reporter gene, whereby dimerization allows isolation of the host cells and selection of the dimerizing polypeptide.

22. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and / or chemical properties, functional characteristics, structure / function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is the isolation of a dimerizing peptide in bacterial cells base on expression of a *HIS3* reporter conferring a growth advantage. The specification at pp. 3-4 suggests that successful use of large libraries in yeast is not feasible. The specification does not disclose the reporter eukaryotic host cells and appropriate reporter genes wherein cells are isolated by virtue of color, fluorescence, luminescence, cell surface tags, or drug resistance and dimerizing peptides are isolated using a DNA library at least  $10^7$  members. The distinguishing characteristics of the claimed genus are not described. The only adequately described species is isolation of a dimerizing polypeptide in bacteria using a *HIS3* reporter gene conferring a selectable growth advantage. Accordingly, the specification does not provide adequate written description of the claimed genus.

23. Vas-Cath Inc. v. Mahurkar, 19 USPQ 2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 116). As discussed above, the skilled artisan cannot envision the reporter genes and eukaryotic cells of the encompassed genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

24. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

25. The Court of Appeals for the Federal Circuit, which held that "a written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or chemical name,' of the claimed subject matter sufficient to distinguish it from other materials.'" *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir 1993).

26. Therefore, only isolation of a dimerizing polypeptide from a DNA library in bacteria using a *HIS3* reporter gene conferring a selectable growth advantage, but not the full breadth of the claim, meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 § 112 is severable from its enablement provision.

***Claim Rejections - 35 USC § 112 Second Paragraph***

27. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

28. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

29. This rejection is necessitated by applicant's amendment to claim 1, filed 2/6/2004, adding the language ~~i—providing~~ introducing a DNA library into a population of host cells under the conditions . . . .

30. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are:

31. Claim 1, and dependent claims 2-9, are rejected as vague and indefinite. Claim 1, line 3, recites the language: "introducing a DNA library into a population of host cells **under conditions**", which renders the claim vague and indefinite, because a person of skill in the art would not know what nexus existed between the fusion protein or reporter



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gene and the introduced DNA library and so would not be reasonably apprised of the metes and bounds of the claimed invention.

32. Claim 1, and dependent claims 2-9, are rejected as vague and indefinite. Claim 1, lines 12-13, recites the language: "wherein dimerization and binding of the fusion protein to the transcriptional regulatory sequence of the reporter gene", which renders the claim vague and indefinite, because it is not clear whether the fusion protein is dimerizing to itself, or dimerizing to the transcriptional regulatory sequence.

***Conclusion***

33. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Shibuya  
Examiner  
Art Unit 1639

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PADMASHRI PONNALURI  
PRIMARY EXAMINER